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(54) DIALYZER

(71) We, TAKEDA YAKUHIN KOGYO KABUSHIKI KAISHA, also known as Takeda Chemical Industries, Ltd., a Japanese Body Corporate, of 27 Doshomachi 2-chome, Higashi-ku, Osaka, Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to a dialyzer. More particularly, the invention relates to a combined dialyzer and adsorber unit for use in an artificial kidney apparatus, which unit has been significantly reduced in size and made portable.

Currently hemodialysis is being used for treating various types of renal insufficiency intoxication with various drugs. In recent years dialysis of blood has been widely practiced, and has by now become essential, for patients with chronic uremia or acute renal failure or cases of drug intoxication. At this time the most commonly used dialysis approach is the use of a cellulose membrane or semi-permeable membranes which allow permeation of molecules up to 36,000 molecular weight. The patient's blood is pumped into a dialyzer and while the blood is in the dialysate membrane chamber the uremic wastes, such as urea, uric acid, creatinine and other toxic substances present in the blood in excess, such as salts, can be dialyzed out through the membrane defining the chamber and picked up in dialysate passing along the other side of the membrane. By application of pressure or osmotic concentration gradients, water can be eliminated from the blood in a controlled fashion.

There are three common types of dialyzers, a parallel plate type in which parallel membranes are arranged between which the dialysate and blood flow, a capillary tube type in which a plurality of capillary tubes are provided for the blood and the dialysate flows over the capillary tubes, and a coil tube in which the blood flows through a coiled tube and the dialysate flows over the outside surfaces of the coils of the tube. It is preferred that all types be disposable after a single use to avoid the necessity of sterilization.

At the present time, for parallel plate and capillary tube type dialyzers, a single pass system of dialysate flow is used, or large dialysate tanks are used and dialysate is recirculated and at periodic intervals the entire bath is changed, or additions are made to the bath and an equal amount discarded. This last mentioned procedure is the commonly used procedure for coils.

The most commonly used dialysate flow rate is 500 cc/min. For six-hour dialysis approximately 200 liters of dialysate is required. Even when attempts are made to reduce the dialysate flow, a 100 liter tank is still needed for most dialysate units. Thus a large amount of dialysate is presently required, and as a result dialysis is costly and a relatively large space is required for the dialysis apparatus.

The idea has recently been advanced to use a chemical absorbent material to remove the uremic wastes while recycling the dialysate fluid and thus to reuse the recycled dialysate.

If the dialysate can be regenerated by utilizing chemical adsorbents to adsorb the uremic wastes and toxic substances from the dialysate, the artificial kidney apparatus can be made smaller and simpler and dialysis can be made less expensive overall. Just as most dialyzers are used once and then discarded, in the regeneration system it is preferred that the chemical adsorbents also be disposable in order to simplify the process further. This requires additional disposable items such as disposable chemical adsorbent cartridges. One such separate adsorbent cartridge is presently available.

If the dialysate regeneration system and the dialyzer, both of which are disposable items, can both be accommodated in a small package, the artificial kidney apparatus can be simpler, less expensive and easier to operate and control.

It is therefore an object of the present invention to provide a combined dialyzer and adsorber unit which is compact and which can be used in a simple artificial kidney

apparatus to permit recirculation of the dialysate and thereby reduce the size and expense of such a system.

It is a further object of the present invention to provide a combined dialyzer and adsorber unit which can be made out of easily moldable plastics material so that such a unit can be made at relatively low cost and can be discarded after a single use.

It is a still further object of the invention to provide a combined dialyzer and adsorber unit which can also be used to generate a charge of dialysate prior to starting dialysis of a patient simply by circulating pure water through the unit.

It is another object of the present invention to provide such a compact dialyzer unit in which the flow of dialysate is branched so as to flow simultaneously through the unit so that dialysate is being passed through the dialyzer for carrying out dialysis and dialysate is also being passed through the adsorbent for removal of the contaminants.

It is yet another object of the invention to provide a dialysis apparatus which includes the dialyzer unit of the invention and means for directing the flow of dialysate in a tank apparatus in which the dialyzer unit of the invention is positioned.

These and other objects of the invention may be achieved by the combined dialyzer and adsorber unit which has a core member and a sleeve member around the core.

In accordance with the invention there is provided a combined dialyzer and adsorber unit comprising a core member and a sleeve member around the core member, one of the members being a dialyzer and the other of the members being an adsorber having an inlet and an outlet, and dialysate distribution means for directing flow of dialysate through the adsorber from the inlet to the outlet and through the dialyzer. Preferably, the sleeve member further comprises an outer wall therearound and defining a chamber within which the remainder of the sleeve member is located.

One of the members may be a dialyzer of the coiled tube type, plate type or capillary tube type, while the other member may be an adsorber in the form of a mass of adsorbent material in a container. Preferably, water soluble dialysate material may be mixed with the adsorbent material in the container, the adsorbent material and the dialysate material both being in the form of granules. The core can be the adsorber and the sleeve the dialyzer, or the sleeve can be the adsorber and the core the dialyzer.

In one embodiment of the unit, a cover is provided over one end of the unit for guiding the flow of dialysate through the unit so that it flows out of the dialyzer and into the adsorber. The unit cover is over the sleeve and one end of the container and spaced from the end of the container sufficiently to give access to the aperture in the cover. Spacing means can be provided on said container extending beyond the end of the container and over which said unit cover engages for keeping the unit cover spaced from the end of the container. The spacing means can be a ring of plastics material having apertures therein and force fitted over the end of said container.

The dialyzer can be a coil tube dialyzer, such as a flat tube of a membrane material permeable to uremic wastes and toxic materials in blood, said tube being wrapped in a coil around said core member, a screen layer between each of the coils of the tube, a blood inlet tube connected to one end of the flat tube and a blood outlet tube connected to the other end of the flat tube, said blood tubes extending to the exterior of the sleeve. Alternatively the dialyzer can be a capillary tube dialyzer or a plate dialyzer.

In another embodiment, a dialyzer distribution chamber is provided on the other end of said unit having a dialysate inlet therein and having apertures opening into an adsorbent chamber containing the adsorbent and a dialyzer chamber containing the dialyzer, whereby dialysate fluid fed into the unit is distributed in a branch flow through the dialyzer and the adsorbent chambers.

The adsorbent chamber can be a cylindrical chamber and said dialysate distribution chamber is mounted on the bottom thereof with the bottom wall of the cylindrical chamber having apertures from the distribution chamber to said adsorbent chamber, and said dialyzer chamber can be an annular chamber having the lower end extending below the bottom of said adsorbent chamber and the apertures from said dialysate distribution chamber opening laterally from the dialysate distribution chamber into said dialyzer chamber.

The unit can have the core member in the form of an adsorbent chamber adapted to contain an adsorbent therein and having a dialysate outlet at one end of the unit, the sleeve member around said core member in the form of a dialyzer, and can have a dialysate distribution chamber on the other end of said unit having a dialysate inlet therein and having apertures opening into said adsorbent chamber and having further apertures opening laterally of said unit for directing a flow of dialysate from the distribution chamber to a position just beneath the dialysate unit. When this embodiment of the unit is stood on its other end in a tank of dialysate, dialysate fluid fed into the

distribution chamber is distributed in a branch flow through the adsorbent chamber and along the dialyzer on the outside of the adsorbent chamber. The adsorbent chamber can be a cylindrical chamber having an annular support member depending from said other end for supporting the unit in a tank of dialysate.

In another embodiment the unit can have a core member in the form of a dialyzer chamber having a dialyzer therein and a dialysate inlet means at one end and a dialysate outlet means at the other end, a first adsorbent chamber on one side of said core member having a dialysate inlet means at one end thereof and aperture means between the other end of said first adsorbent chamber and the corresponding end of the dialyzer chamber, and a second adsorbent chamber on the other side of said dialyzer chamber having a dialysate outlet at the end corresponding to the other end of the first adsorbent chamber and aperture means between the end corresponding to the one end of the first adsorbent chamber and the corresponding end of the dialyzer chamber, whereby dialysate fluid fed into the unit flows first through the first adsorbent chamber from end to end, then from one end of the dialyzer chamber to the other, and then through the second adsorbent chamber from end to end. The dialyzer chamber can be a cylindrical chamber and the adsorbent chambers can be annular semicylindrical chambers fitting closely around said dialyzer chamber. Preferably the dialyzer is a tube dialyzer comprising a plurality of tubes of semipermeable membrane material extending from end to end of the dialyzer chamber, the space around said tubes being the space through which the dialysate passes.

The parts of the unit can be made of plastic so that they are inexpensive and the unit can be discarded after a single use. The adsorber can have mixed in with the adsorbent material or in a separate compartment a water soluble dialysate material which can be dissolved in water to make a dialysate for use with the unit by circulating water through the unit prior to using the unit for dialysis. The separate compartment can be a dialysate material cup positioned inside said container and having an aperture in the bottom thereof for permitting liquid to pass through the cup, and a water soluble dialysate material in said cup. The cup can be a moldable plastics material inert to the dialysate.

The invention will now be illustrated by way of example with reference to the accompanying drawings, in which:

Fig. 1 is a perspective view, partly in section, of a first embodiment of the combined dialyzer and adsorber unit according to the invention;

Fig. 2 is a vertical section taken on the line 2—2 of Figure 1;

Fig. 3 is a transverse section taken on line 3—3 of Fig. 1;

Fig. 4 is a diagram showing one way of using the combined dialyzer and adsorber unit of the invention in an artificial kidney apparatus;

Fig. 5 is a schematic sectional view of a slightly modified form of the unit shown in Fig. 1 and illustrating a reverse direction of flow from that of the unit of Fig. 1 as connected in Fig. 4;

Fig. 6 is a schematic sectional view of a still further embodiment of the dialyzing unit of the present invention;

Fig. 7 is a diagramatic view of one way of using the unit of Fig. 6 in an artificial kidney apparatus;

Fig. 8 is a side elevation view of still another embodiment of the dialyzing unit of the present invention in which hollow-fiber semi-permeable membranes are used;

Fig. 9 is a view similar to Fig. 2 of a modified embodiment of the unit;

Fig. 10 is a view similar to Fig. 2 of a further modified embodiment of the unit;

Fig. 11 is a schematic sectional view of another embodiment of the dialyzing unit employing hollow-fiber semi-permeable membranes; and

Figs. 12 and 13 are graphs showing the results of experimental dialysis performed using the dialyzing units illustrated in Figs. 5 and 6, respectively.

Referring first to Figs. 1—3, the combined dialyzer and adsorber unit comprises a core generally indicated at 10 and a sleeve generally indicated at 11, and in the embodiment shown, the core 10 is constituted by an adsorbent material 12, the nature of which will be described in greater detail hereinafter, the adsorbent material being contained in a right circular cylindrical container 13. The container 13 has a bottom cover 14 threaded onto the bottom end of the container 13 and the cover has a downwardly extending conical portion 15 at the apex of which is a tubular outlet 16. Depending from the edge of the cover 14 is a depending ring 18 which has apertures 19 therein, here shown as slots extending upwardly from the bottom edge of the ring 18. At the top of the container 13 is a top end wall 20, here shown as being integral with the cylindrical portion of the container 13, and at the center of the top wall is an exteriorly threaded neck 21. A top cover 22 having an inlet aperture 22a in the top thereof is threaded onto the neck 21. Held between the bottom cover 14 and the bottom end of the cylindrical portion of the container 13 is a porous bottom retainer plate 17, and held between the top cover 22 and the top of the neck 21 is a gasket 23, and

two porous top retainer plates 24 and 25. The porous retainer plates can of course also function as filters for filtering at least some of the solid material from the liquid passing through them.

A spacer means in the form of a top ring 26 is force fitted over the outside of container 13 at the top thereof and projects above the top of the top cover 22. Apertures 27 are provided in this ring 26.

The sleeve 11 in the present embodiment is constituted by a dialyzer, and more specifically by a coil tube type dialyzer generally indicated at 30. The dialyzer 30 is made up of a wide flat tube 31 of a membrane material which is permeable to molecules up to 36,000 molecular weight, the most commonly used type being a cellulose material membrane, such as Cellophane (registered Trade Mark), Cuprophane or cellulose acetate. Between the turns or spirals of the tube 31 are layers of screen 32, which layers act to space the walls of adjacent turns of the tube from each other to permit liquid to pass over the outsides of the walls of the tube. Attached to one end of the tube 31 is a blood inlet tube 33 having a coupling 33a on the free end thereof, and the tube 33 is led downwardly along a groove in a crescent shaped holder 34 which is placed against the outer surface of the container 13 prior to the start of the coiling of the tube 31 thereon. Similarly a blood outlet tube 35 having a coupling 35a on the free end thereof is attached to the other end of the tube 31 and is led downwardly along a groove in a second crescent shaped holder 36 placed against the outside of the coiled tube 31. The blood inlet and outlet tubes 33 and 35 extend downwardly and out of the bottom of the dialyzer.

Fitted tightly over the dialyzer 30 is an enclosure means, here shown as a cover 37, which holds the coiled tube 31 in place, and which also extends upwardly over the top of the ring 26 so as to completely enclose the space above the top of the dialyzer 30 and the container 13.

One manner in which the combined dialyzer and adsorber unit described above can be used in an artificial kidney apparatus is shown diagrammatically in Fig. 4. A tank 38 is provided for holding the required amount of dialysate 39 to carry out a dialysis of a patient. Mounted on one wall of the tank 38 is a holder mount M which has secured thereto an open topped unit holder H in which the combined dialyzer and adsorber unit is positioned with the depending ring 18 resting on the bottom of the holder H. The blood inlet and blood outlet tubes 33 and 35 are led upwardly along the outside of the combined dialyzer and adsorber unit out of the top of the holder H and attached to the patient. Extending from the bottom of the tank 38 to the bottom of the holder H is an intake line Li, and connected to the outlet 16 through the bottom of the holder H is a suction line Ls which leads to the suction side of the pump P. From the discharge of the pump P a return line Lr leads back to the tank 38. Appropriate valves (not shown) can be provided in the various lines.

In operation, dialysate 39 from the tank 38 is allowed to flow into the unit holder H, where it will reach the same level as in the tank 38. Thereupon the pump P is started to create a negative pressure in the container 13. Dialysate will thus be drawn upwardly through the spaces between the coils of the tube 31 which are defined by the screen layers 32, passing over the outer surfaces of the coils of the tube 31. Blood from the patient is pumped by suitable means through the interior of the tube 31 at the same time. The uremic wastes and toxic substances in the blood will permeate thorugh the wall of the tube 31 and be picked up by the dialysate. Thus contaminated dialysate will be drawn upwardly out of the top of the dialyzer 30 and through the apertures 27 in the top ring 26 and into the interior of the container 13 throung the cover inlet aperture 22a and porous retainer plates 24 and 25. The dialysate will further be drawn down through the mass of adsorbent 12 and out through the porous bottom retainer plate 17 and the outlet 16 to the pump P through the suction line Ls. From the pump it will be pumped through the return line Lr to the tank 38.

As the contaminated dialysate is drawn through the mass of adsorbent 12, the contaminants will be adsorbed and the dialysate cleaned, so that it can be recirculated.

The particular embodiment described above is intended to be a so-called throw-away unit, and to this end the container 13 and associated parts are made of easily moldable plastic which is also inert to the dialysate, for example polyethylene. If it is desired to make the unit such that it can be reused by periodically refilling the container with adsorbent and sterilizing the unit, while a moldable plastic can be prepared which will withstand several uses, it might be preferable to use a metal such as stainless steel. As discussed above, the tube 31 can be cellulose, such as cellophane, the most commonly used membrane material. The screen layers 32 can also be plastic, for example polypropylene. The tubing is likewise preferably plastic, for example polyvinylchloride. The cover 37 can be any material which will fit tightly over the outside of the dialyzer. Preferably, however, the cover is a clear plastic, such as clear polyethylene, so that a visual check can be made on the dialysate flowing through the unit

to make sure that no blood is leaking from the tube 31 into the dialysate.

The cover 37 has been shown as a shaped cover, for example molded. However, the expense can be reduced somewhat by making the cover 37 a flexible plastics bag. The spacer means in the form of the top ring 26 becomes especially important in such a variation, since it keeps the bag from the top of the cover 22 thereby keeping the aperture 22a open for the passage of the dialysate therethrough.

The retainer plates 17, 24 and 25 can be any common filter material from which a substantially rigid plate can be made, such as molded fiberglass, or plastic, and which is inert to the dialysate.

As the chemical adsorbent, the major ingredient is activated carbon. This activated carbon has the capability of adsorbing organics such as creatinine or uric acid. Activated carbon 10—200 mesh (Tyler Equivalent Designation) in size, especially 16—100 mesh, is desirable. In order to prevent microparticles passing into the dialysate or fragmentation of the charcoal or to keep the surface area of the charcoal large, or to prevent excessive pressure drops in the device, the adsorbent is preferably in a granular form. Alternatively, activated carbon paper which is prepared by incorporating activated carbon powder in a paper web may be employed. This carbon can also be made as a fiber. An additional chemical adsorbent that can be used is aluminum oxide, which is specific for the removal of inorganic phosphate. Any chemical adsorbent, particularly for a specific need, can be placed in this container. Other possibilities would be ion exchange resins, and compounds capable of removing urea as oxidized starch, and urea binders. The mixture and amount of the chemical adsorbent utilized depends upon the patient's need for certain metabolites or drugs to be removed from the blood. In addition to these passive adsorbents mentioned, an active adsorbent system such as enzymes could also be used in the container.

Many variations in the structure of the present device are possible without departing from the scope of the invention. For example, the inlet aperture 22a in the top cover is shown as being in the top thereof, thereby making it necessary to insure that the cover 37 is kept clear of the top 22. By making the structure such that the openings in the upper end of the container are lateral openings the necessity for a spacer means can be eliminated. Moreover, the provision of a removable cover at the upper end of the container is not necessary as long as there is a removable cover at the bottom of the container, and vice versa. In the preferred embodiment, the dialyzer is shown and described as a coil tube dialyzer. However, a parallel plate type dialyzer or a capillary type tube dialyzer could easily be designed in the form of a sleeve which could be placed on the container 13 as the core in place of the coil tube type dialyzer 30. The blood inlet and outlet tubes 33 and 35 could extend upwardly instead of downwardly, and be sealed in cover 37.

The combined dialyzer and adsorbent unit as shown in Fig. 4 is very similar to that of Figs. 1—3, except for the cover 37 of Figs. 1—3. It has a core in the form of the cylindrical container 13a with the dialysat inlet 16a at the bottom thereof and the mass of adsorbent 12a contained withi the container 13a between porous members 17a and 25a, and a top wall 20a with a dialysate outlet 21a therein. It further has the sleeve in the form of the coil tube dialyzer 30a having the flat tube 31a with the layers of screen 32a between the turns of the flat tube 31a, and the blood inlet and outlet tubes 33b and 35b. However, instead of the cover 37, a cylindrical outer wall 37a is provided around the dialyzer 30a which defines a chamber within which the dialyzer is positioned. Inlets 27a and outlets 27b are provided at the top and bottom of this chamber.

In use the unit can be provided with a cover (not shown) over the upper end, and the dialysate inlet can be connected to the inlet 16a, in which case the unit functions in the same way as the unit of Figs. 1—.3. Alternatively, it can be positioned in a tank such as the tank 38 of Fig. 4 with the outlet 21a and inlets 27a submerged, and outlets 27b connected to circulating means, in which case the dialysate will, by the effect of negative pressure, be cleansed as it goes through the adsorber and will simply be discharged into the body of dialysate 39 in the tank 38. The circulating means will draw dialysate downwardly through the dialyzer 30a for carrying out the dialysis. This arrangement makes it possible to have different rates of flow through the adsorbent and the dialyzer where this will promote efficiency in operation of the unit.

Referring now to Fig. 6, there is shown a unit which can be hooked up in an apparatus like that of Fig. 4, but which will produce the different rates of flow through the adsorber and the dialyzer. In Fig. 6, a generally cylindrical adsorbent chamber 40 containing an adsorbent material 47 forms a core. Around the core is a sleeve which is a dialyzer 44, which in this embodiment is a coil tube type dialyzer having a tubular semipermeable membrane 44a and a plastics material mesh sheeting 43 wound in alternating layers. A space 45 is defined between an outer cylinder 46 and a cylinder wall 40a forming the core and which is closed by end walls 46a and 46b connected

to inner cylinder wall 40a. Support member 46c depends from end wall 46b. The blood is introduced though an inlet 42a connected to one end of the tubular membrane 44a and the dialyzed blood is discharged from an outlet 42b connected to the other end of the tubular membrane 44a. On the bottom of the adsorbent chamber 40 is a dialysate distribution chamber 45a defined by the extension of wall 40a and end wall 46b. Dialysate inlet 45b opens into distribution chamber 45a. Apertures 45c open from the distribution chamber 45a to space 45, and outlets 49 are provided in end wall 46a at the top of the sleeve. A porous wall 40b closes the bottom of chamber 40. Adsorbent material 47 is contained in a porous membrane 47a and substantially fills chamber 40.

In operation, the dialysate enters through the dialysate inlet 45b into the distribution chamber 45a, wherein a portion of dialysate is directed into chamber 45 and the remainder into adsorbent chamber 40. The dialysate, after flowing through the adsorbent 47, overflows at the top. The dialysate directed into the chamber 45 flows along the faces of tubular membrane 44a dialyzing the blood and, then, overflows through the dialysate outlet 49.

As illustrated in Fig. 7, such a unit can be installed in a fluid tank 38a, and the dialysate 39a overflowing from chamber 40 and outlets 49 flows into the body of dialysate in fluid tank 38a. Pump means Pa draws dialysate from the tank and pumps it through pipe Li to the dialysis unit. The dialysis unit can be removably installed in the fluid tank and, after use, either the entire unit or the adsorbent material 47 and the membrane in which it is enclosed alone can be discarded.

With this arrangement, it is possible, by correctly proportioning the aperture 45c and porous wall 40b to control the rates of flow of dialysate through the adsorbent 47 and over the dialysis tube of the dialyzer 44 to produce the most desirable rates. It is often the case that the rate of flow through the adsorption material 47 to achieve optimum adsorption is less than that for the flow of the dialysate over the tubular membrane 44a to achieve optimum dialysis. By utilizing the structure as described above for Figs. 6 and 7, the optimum flow rates for both flows can be achieved in the same apparatus.

The unit illustrated in Fig. 8 is similar to that of Figs. 6 and 7 and is designed to be used in substantially the same way. It has the core with the cylinder wall 40b and which contains the adsorbent. The support member 46c depends from the cylinder wall 40a and the apertures 45c open laterally out of the distribution chamber 45a, in this instance in four directions. In the particular construction illustrated, the wall of the cylinder defining the distribution chamber is spaced slightly inwardly of the support member 46c, so that the apertures must be extended at 45d through the support member 46c. The dialyzer 44 in this embodiment is a capillary tube type dialyzer in which the tubes are wrapped around the core. The flexible blood inlet tube 42a extends from the inlet and the flexible blood outlet tube 42b extends from the outlet.

The use of the unit of Fig. 8 is the same as that of Fig. 6. It is positioned in a tank as shown in Fig. 7 in the same manner as the unit of Fig. 6, and the dialysate is pumped into the inlet 45b. The flow of the dialysate through the adsorber is the same as for the unit of Fig. 6. However, when the unit of Fig. 8 is positioned by itself in the tank, flow of the dialysate over the dialyzer 44 is by convection currents flowing upwardly along the dialyzer from the openings 45d.

If it is desired to improve the flow of dialysate along the sides of the cylinder wall 40a over the tubes of the capillary tube dialyzer 44, a sleeve similar to the outer cylinder 46 can be placed over the dialyzer 44, in which case the unit would be substantially the same as that of Fig. 6 except for the specific form of dialyzer.

In all of the embodiments described thus far, the dialyzer has been positioned as a sleeve around an adsorber which is the core for the dialyzer sleeve. It is clear that with minor changes in design the two elements can be reversed, i.e., the dialyzer can be positioned within a sleeve in the form of an adsorber to serve as the core for the adsorber. One such arrangement is shown in Fig. 9.

As seen in Fig. 8, the unit comprises a container 50 which is generally a right circular cylinder, and on the outside thereof is a bottom wall 52 from the outer edge of which extends an outer wall 51 generally concentric to the container 50. There is defined within these walls an annular sleeve which is filled with an adsorbent 57. The bottom wall has a series of apertures 53 therein, and in the bottom of the annular sleeve is a porous retainer plate 53a. This plate is held in position by the weight of the adsorbent 57. Over the top of the sleeve is an annular top cover 54 which is threaded onto the outer wall 51, and which holds an annular porous retainer plate 56 against the top of the wall 51. The top cover 54 also has a series of apertures 55 therein.

Threaded onto the lower end of the outer wall 51 is an annular bottom cover 58 having an outer wall 58a and an inner wall 58b. The top end of the outer wall is in threaded engagement with the bottom end of the outer wall 51, and the top end of the inner wall

58b presses a gasket 59 against the bottom surface of the bottom wall around the bottom of the container 50. At one point around the circumference of the bottom cover 58 is an outlet 60. Projecting downwardly at intervals around the circumference of the inner wall 58b are legs 58c.

Within the container 50 is a dialyzer 61, the details of which are not shown, which can be the same as that shown in Figs. 1—3, i.e., having a tube with layers of screen between the turns of the coiled tube, or can be a capillary or flat tube type. Actually the latter is precfrred in this embodiment. A bottom plug 64 is threaded into the lower end of the container 50, and it has a neck 64a thereon which is covered by a bottom dialyzer eover 65 threaded thereon and having a bottom dialyzer aperture 65a therein. A porous bottom dialyzer retainer plate 66 can, if desired, be provided inside the cover 65, being held against the neck 64a by the cover 65. A blood inlet tube 70 extends through the plug 64 to one end of the dialyzer 61, and a blood outlet tube extends through the retainer plate 66 from the other end of the dialyzer 61. The top of the container 50 is closed by a top dialyzer cover 62 threaded onto the top end of the container 50, the top dialyzer eover having an outlet aperture 62a therein and holding a porous retainer plate 63 against the top end of the container 50. Finally a cover 71 is fitted tightly over the outside of the sleeve, the cover here being shown as a rigid cover which extends upwardly above the top of the container 50. If a flexible material cover is used, some spacer means such as the top ring 26 of Figs. 1—3 must be used.

This embodiment of the unit can be used in the same manner as that of Figs. 1—3, that is the suction pump is attached to the outlet 60 and dialysate is supplied to the holder in which the unit is positioned. The dialysate is drawn upwardly through the container 50 and the dialyzer 61 therein, overflows through the aperture 62a in the cover 62 and is then drawn downwardly through the adsorbent 57 in the sleeve. The thus cleansed dialysate is collected in the bottom cover 58 and drawn out through the outlet 60.

If a configuration more nearly like that of Figs. 1—3 is used, i.e., with a conical portion and neck at the bottom of the container, the pressure side of the pump can be connected to pump dialysate first through adsorbent 57.

The unit can be modified further to provide a charge of a water soluble dialysate material in an amount such that when a predetermined amount of water is circulated through the unit, the desired amount of dialysate is automatically prepared. One way to do this is in the embodiments described thus far is simply to mix in with the adsorbent material the desired amount of soluble dialysate material, and then prior to starting the flow of blood from the patient through the dialyzer to pump pure water in an amount equal to the amount of dialysate required through the unit until the soluble dialysate material is completely dissolved. However, some dialysate materials should not be stored in contact with the adsorbent materials. An embodiment of the unit in which the dialysate material is kept separate from the adsorbent material is shown in Fig. 10.

In Fig. 10, the structure of the unit is essentially the same as that of Figs. 1—3. However, there has been added to the interior of the container 50 a dialysate material cup 80. This cup has a lip 81 which is held between the retainer plate 17 and the end of the container 50. The wall of the cup extends along the inside of the wall of the container 50 and has a threaded neck 80a thereon over which is threaded a cup cover 82 having an aperture 82a therein. A porous retainer plate 83 is held between the cover 82 and the neck 80a. The anhydrous soluble dialysate material is placed in the cup, and when water is passed through the unit prior to its operation as a dialysis unit, the water dissolves the dialysate material after which the cup 80 remains empty for the rest of the time the unit is in use.

The advantages of such an arrangement are many. The provision of the proper amount of dialysate material in the unit eliminates the need to have a specially trained person prepare thedialysate for use in the unit. A relatively untrained person can install the unit in the artificial kidney apparatus and circulate a measured amount of water through the unit before starting to dialyze the patient.

Moreover, combined dialyzer and adsorbent units can be made up ahead of time for different types of dialysis.

A further modification of the unit of the invention is shown in Fig. 11. A cylindrical dialysis chamber 95 is provided as a core for the unit and has an outer cylindrical wall 114. Around the dialysis chamber 95 are two matching semi-annular adsorbent chambers 96 having an inner cylindrical wall 96a fitting tightly against the outer cylindrical wall 114. Within the dialysis chamber 95 is a dialyzer which is made up of a plurality of hollow-fiber semi-permeable membranes 109 extending parallel to the axis of the cylinder and having the ends mounted on and sealed to mounting members 110 at the opposite ends of the chamber 95. Thus the passages through the fiber membranes 109 constitute passages for the blood being dialyzed, while the space around the membranes 109 within the chamber 95 consti-

tutes a space for the flow of dialysate over the outer surfaces of the membranes 109. A blood inlet 92 is provided at one end of the membranes 109. A blood inlet 92 is provided at one end of the chamber 95 while a blood outlet 93 is provided at the other end of the chamber 95.

Each of the semi-annular chambers 96 constitutes an adsorbent chamber 100 which is filled with adsorbent 97. A dialysate inlet 101 is provided at one end of one of the adsorbent chamber 100 while a dialysate outlet 102 is provided at the other end of the other adsorbent chamber 100. Filters 99 are for the inlet 101 and outlet 102. At the opposite end of the one adsorbent chamber 100 from the dialysate inlet 101 is a lateral aperture 98 which extends through both the inner wall 96a of the chamber 96 and also through the cylindrical wall 114 of the dialysate chamber 95. This aperture is filled by a filter member 98a. A similar opening 98 is provided at the other end of the other adsorbent chamber 100 from the dialysate outlet 102, and this is also filled by a filter member 98a.

With this arrangement, blood flowing into the inlet 92 will flow through the hollow fiber membranes 109 and out the outlet 93. This inlet and outlet are of course connected to the source of blood to be dialyzed. Dialysate, on the other hand, is pumped into the unit through inlet 101 whereupon it flows in sequence through the adsorbent in the semi-annular chamber 100, through the dialysis chamber 95 over the surfaces of the membranes, and then through the adsorbent in the other semi-annular chamber. By placing the first aperture 98 at one end of the dialysis chamber 95 and the second aperture 98 at the other end, flow of the dialysate diagonally across the chamber 95 is ensured, thus ensuring that the dialysate spends the maximum amount of time in the chamber 95 and that fresh dialysate flows in all parts of this chamber. The dialysate flow into the unit is first subjected to adsorption before it flows across the membranes, thereby removing any residual impurities therefrom, and is again subject to adsorption immediately after it has flowed over the membranes.

In use this unit can be hooked into a dialysis apparatus in a way generally similar to that shown in Fig. 7 for the embodiment of Fig. 6. The unit is preferably placed in a separate tank from the dialysate, however, and the blood tubes are hooked to the blood inlet 92 and blood outlet 93 respectively.

It will be understood that while only a single dialysate inlet 101 and a single dialysate outlet 102, and single apertures 98 are shown, it is within the scope of the invention to provide a plurality of such openings in order to speed the flow of dialysate and spread it more evenly throughout the apparatus.

The semi-permeable membranes employed in the blood dialyzing units thus far illustrated and described can be the same as those described in connection with the embodiment of Figs. 1—3, and the adsorbent can also be the same as that described in connection with that embodiment. Further, as said adsorbent, alumina gel may be used in combination with activated carbon. For example, such alumina gel may be prepared by adding an alkali (e.g., an alkali derived from ammonia or calcium carbonate) to an aqueous solution of an aluminum salt (e.g., aluminum sulfate, aluminum chloride and other mineral acid salts) to neutralize the latter while the resultant salt and other solubles are removed by rinsing to cause an alumina sol to form, maintaining the sol in a hydrophobic medium (e.g., hydrocarbon, halogenated hydrocarbon, spindle oil, etc) at an elevated temperature (e.g., 70° to 100°C) and thereby ripening it to gel and, finally drying the same.

Several experiments were run using certain of the units described hereinbefore, as follows:

Experiment 1

An experimental dialysis of blood was performed using the dialyzing unit illustrated in Fig. 6. The conditions used are as follows:

(a) Dialysate fluid: 30 liters [AK Solita (Shimizu Seiyaku Co., Ltd.), 1 - in - 35 dilution, 37°C]

(b) Flow rate of dialysis: 5 liters/min. (semi-permeable membrane), 0.5 liters/min. (adsorbent)

(c) Simulated blood: The same dialysate supplemented with 18 milligrams/dl. of creatinine

(d) Flow rate of simulated blood: 200 milliliters/min.

(e) Fluid tank and pump means:
Fluid tank : 40 cm in diameter and 40 cm in height
Drive means: A single rotor screw pump

Operating flow : 19 liters/minute (60 cycles)
Operating head: 3.0 meters H_2O (60 cycles)

(f) Activated carbon: Steam-activated coconut shell granular carbon, 48 to 20 mesh, 500 grams.

(g) Semi-permeable membrane: Bemberg Cuprophan (trade name of West Germany), 0.8 square meters.

(h) Control apparatus: A commercial coil-type dialyzer in combination with a circulation-type dialysate supply unit for artificial kidney use.

The test result is graphically presented in Fig. 12, where the creatinine concentration of the simulated blood on the vertical axis is plotted against the dialyzing time on the horizontal axis.

It will be seen that whereas the control apparatus began to show an attenuation of concentration drop about 3 hours after the start of dialysis (the triangular marks), the blood dialysis apparatus of the present invention shows a more constant concentration decrease (the circular marks). Thus, whereas the control apparatus requires a dialyzing time of 5 hours, the apparatus of the present invention achieves the same result in 3 hours.

EXPERIMENT 2

Using the dialyzing unit illustrated in Fig. 6, an experiment similar to that of Experiment 1 was performed, except that the creatinine concentration of the simulated blood used was 17.2 milligrams per dl.

The result is as shown in Fig. 13, which shows that the dialysis achieved by the control apparatus in 5 hours (the cross marks) can be accomplished by the apparatus of the present invention in 2.6 hours.

It will be seen that there has been provided a simple yet compact unit which is easy to use and can be used in many different types of dialysis. By recirculating dialysate through the unit, the amount of dialysate needed can be greatly reduced. The heretofore unused space in a coil tube dialysis unit has been utilized, thereby making the overall unit more compact and portable. The unit can be used in simple apparatus such as an open tank or a tank with a separate holder for the unit. By making the device out of inexpensive materials, not only can the cost be reduced but the unit can be made as a throw-away unit, thereby avoiding the necessity for sterilizing, and recharging with adsorbent and thus reducing the time and labor involved in carrying out dialysis. By providing the dialysate material in a premeasured amount in a water-soluble form within the unit, not only is the need for specially trained personnel minimized, but an opportunity for mistakes in the preparation of the dialysate is eliminated.

WHAT WE CLAIM IS:—

1. A combined dialyzer and adsorber unit comprising a core member and a sleeve member around the core member, one of the members being a dialyzer and the other of the members being an adsorber having an inlet and an outlet, and dialysate distribution means for directing flow of dialysate through the adsorber from the inlet to the outlet and through the dialyzer.

2. A combined dialyzer and adsorber unit as claimed in claim 1 in which the sleeve member further comprises an outer wall therearound and defining a chamber within which the remainder of the sleeve member is located.

3. A combined dialyzer and adsorber unit as claimed in claim 1 or claim 2 comprising a core member and a sleeve member around the core member, one of the members being a dialyzer and the other of the

members being an adsorber container having an inlet and an outlet, and a unit cover over the sleeve and the end of the core member for guiding dialysate fluid from the dialyzer into the adsorber.

4. A combined dialyzer and adsorber unit as claimed in claim 3 in which the core member is the adsorber container and the sleeve is the dialyzer.

5. A combined dialyzer and adsorber unit as claimed in claim 4 in which the adsorber container is a cylindrical container having an apertured top cover and an apertured bottom cover and the unit cover being over the sleeve and one end of the container and being spaced from the cover on the end of the container sufficiently to give access to the aperture in the cover.

6. A combined dialyzer and adsorber unit as claimed in claim 5 in which the container and covers are of a moldable plastic inert to the dialysate.

7. A combined dialyzer and adsorber unit as claimed in claim 5 or claim 6 further cocprising a spacing means on the container extending beyond the cover on the end of the container and over which the unit cover engages for keeping the unit cover spaced from the container cover.

8. A combined dialyzer and adsorber unit as claimed in claim 7 in which the spacing means is a ring of plastic having apertures therein and force fitted over the end of the container.

9. A combined dialyzer and adsorber unit as claimed in any one of claims 5 to 8 further comprising a mass of adsorbent material in the adsorber container.

10. A combined dialyzer and adsorber unit as claimed in claim 9 further comprising water soluble dialysate material in the container mixed with the adsorbent material, the adsorbent material and dialysate material both being in the form of granules.

11. A combined dialyzer and adsorber unit as claimed in claim 9 further comprising a dialysate material cup positioned inside the container and having an aperture in the bottom thereof for permitting liquid to pass through the cup, and a water soluble dialysate material in said cup.

12. A combined dialyzer and adsorber unit as claimed in claim 11 in which the cup is a moldable plastics material inert to the dialysate.

13. A combined dialyzer and adsorber as claimed in claim 4 in which the dialyzer is a coil tube dialyzer.

14. A combined dialyzer and adsorber unit as claimed in claim 13 in which the coil tube dialyzer comprises a flat tube of a membrane material permeable to uremic wastes and toxic materials in blood, the tube being wrapped in a coil around the core member with a screen layer between each of the coils of the tube, a blood inlet tube connected to one end of the flat tube and a blood outlet tube connected to the other end of the flat tube, the blood inlet and outlet tubes extending to the exterior of the sleeve.

15. A combined dialyzer and adsorber unit as claimed in claim 3 in which the dialyzer is a coil tube dialyzer.

16. A combined dialyzer and adsorber as claimed in claim 3 in which the dialyzer is a capillary tube dialyzer.

17. A combined dialyzer and adsorber as claimed in claim 3 in which the dialyzer is a plate dialyzer.

18. A combined dialyzer and adsorber as claimed in claim 3 in which the core member is the dialyzer and the sleeve member is the adsorber.

19. A combined dialyzer and adsorber unit as claimed in claim 3 further comprising a mass of adsorbent material in the adsorber container.

20. A combined dialyzer and adsorber unit comprising a core member and a sleeve memebr around said core member, one of the members being a dialyzer chamber having a dialyzer therein and a dialysate outlet at one end of the unit, and the other of the members being an adsorbent chamber adapted to contain an adsorbent therein and a dialysate outlet at said one end, and a dialysate distribution chamber on the other end of the unit having a dialysate inlet herein and having apertures opening into the adsorbent chamber and the dialyzer chamber, whereby dialysate fluid fed into the unit is distributed in branch flow through the dialyzer and the adsorbent chambers.

21. A combined dialyzer and adsorber unit as claimed in claim 20 in which the core member is the adsorbent chamber, and the sleeve member is the dialyzer chamber having the dialyzer therein.

22. A combined dialyzer and adsorber unit as claimed in claim 20 in which the adsorbent chamber is a cylindrical chamber and the dialysate distribution chamber is mounted on the bottom thereof with the bottom wall of the cylindrical chamber having apertures from the distribution chamber to the adsorbent chamber, and the dialyzer chamber is an annular chamber having the lower end extending below the bottom of the adsorbent chamber and the apertures from the dialysate distribution chamber opening laterally from the dialysate distribution chamber into the dialyzer chamber.

23. A combined dialyzer and adsorber unit as claimed in claim 22 in which the dialyzer is a coil tube dialyzer having a flat tube of a membrane material permeable to uremic wastes and toxic materials in blood, the tube being wrapped in a coil within the dialysate chamber around the core member with a mesh material between each of the

coils of the tube, and a blood inlet tube connected to one end of the tube, and a blood inlet tube connected to one end of the flat tube and a blood outlet tube connected to the other end of the flat tube, the blood inlet and outlet tubes extending to the exterior of the unit.

24. A combined dialyzer and adsorber unit as claimed in claim 20 in which the core memebr is the dialyzer chamber having the dialyzer therein and the sleeve member is the adsorbent chamber.

25. A combined dialyzer adsorber unit as claimed in claim 20 further comprising a mass of adsorbent in the adsorbent chamber.

26. A combined dialyzer and adsorber unit comprising a core member in the form of an adsorbent chamber adapted to contain an adsorbent therein and having a dialysate outlet at one end of the unit, a sleeve member around the core member in the form of a dialyzer, and a dialysate distribution chamber on the other end of the unit having a dialysate inlet therein and having apertures opening into the adsorbent chamber and having further apertures opening laterally of the unit for directing a flow of dialysate from the distribution chamber to a position just beneath the dialysate unit, whereby when the unit is stood on said other end in a tank of dialysate, dialysate fluid fed into the distribution chamber is distributed in a branch flow through the adsorbent chamber and along the dialyzer on the outside of the adsorbent chamber.

27. A combined dialyzer and adsorber unit as claimed in claim 26 in which the adsorbent chamber is a cylindrical chamber having a support member depending from said other end for supporting the unit in a tank of dialysate.

28. A combined dialyzer and adsorber unit as claimed in claim 27 in which the support member is an annular member, and the further apertures extend through said annular member.

29. A combined dialyzer and adsorber unit as claimed in claim 26 in which the dialyzer is a capillary tube dialyzer in which the capillary tubes extend in the direction around the adsorbent chamber.

30. A combined dialyzer and adsorber unit as claimed in claim 26 further comprising a mass of adsorbent in the adsorbent chamber.

31. A combined dialyzer and adsorber unit comprising a core member in the form of a dialyzer chamber having a dialyzer therein and a dialysate inlet means at one end and a dialysate outlet means at the other end, a first adsorbent chamber on one side of the core member having a dialysate inlet means at one end thereof and aperture means between the other end of the first adsorbent chamber and the corresponding end of the dialyzer chamber, and a second adsorbent chamber on the other side of the dialyzer chamber having a dialysate outlet at the end corresponding to the other end of the adsorbent chamber and aperture means between the end corresponding to the one end of the first adsorbent chamber and the corresponding end of the dialyzer chamber, whereby dialysate fluid fed into the unit flows first through the first adsorbent chamber from end to end, then from one end of the dialyzer chamber to the other, and then through the second adsorbent chamber from end to end.

32. A combined dialyzer and adsorber unit as claimed in claim 31 in which the dialyzer chamber is a cylindrical chamber and the adsorbent chambers are semi-annular chambers fitting closely around the dialyzer chamber.

33. A combined dialyzer and adsorber unit as claimed in claim 31 in which the dialyzer is a tube dialyzer comprising a plurality of tubes of semi-permeable membrane material extending from end to end of the dialyzer chamber, the space around said tubes being the space through which the dialysate passes.

34. A combined dialyzer and adsorber unit as claimed in claim 31 further comprising a mass of adsorbent in each of the adsorbent chambers.

35. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figures 1 to 4.

36. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figure 5.

37. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figures 6 and 7.

38. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figure 8.

39. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figure 9.

40. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figure 10.

41. A combined dialyzer and adsorber unit substantially as hereinbefore described with reference to and as illustrated in Figure 11.

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1470206 COMPLETE SPECIFICATION

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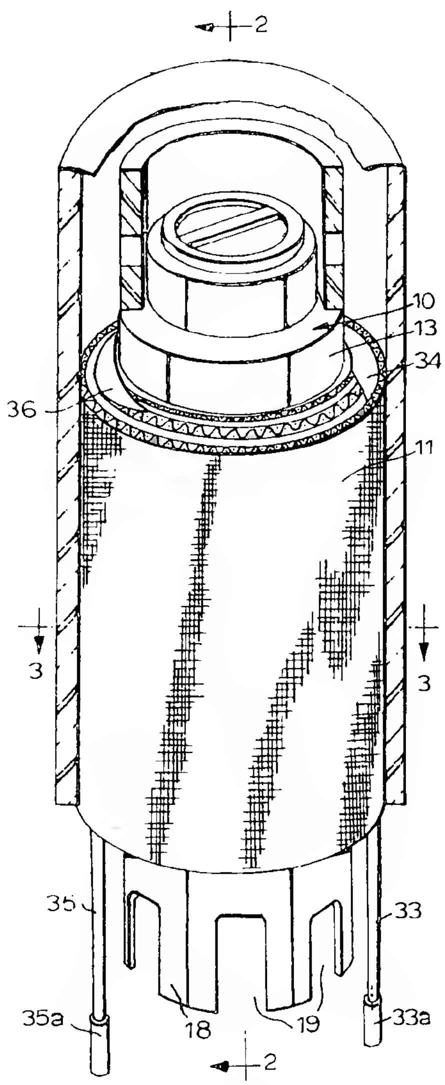

FIG.1

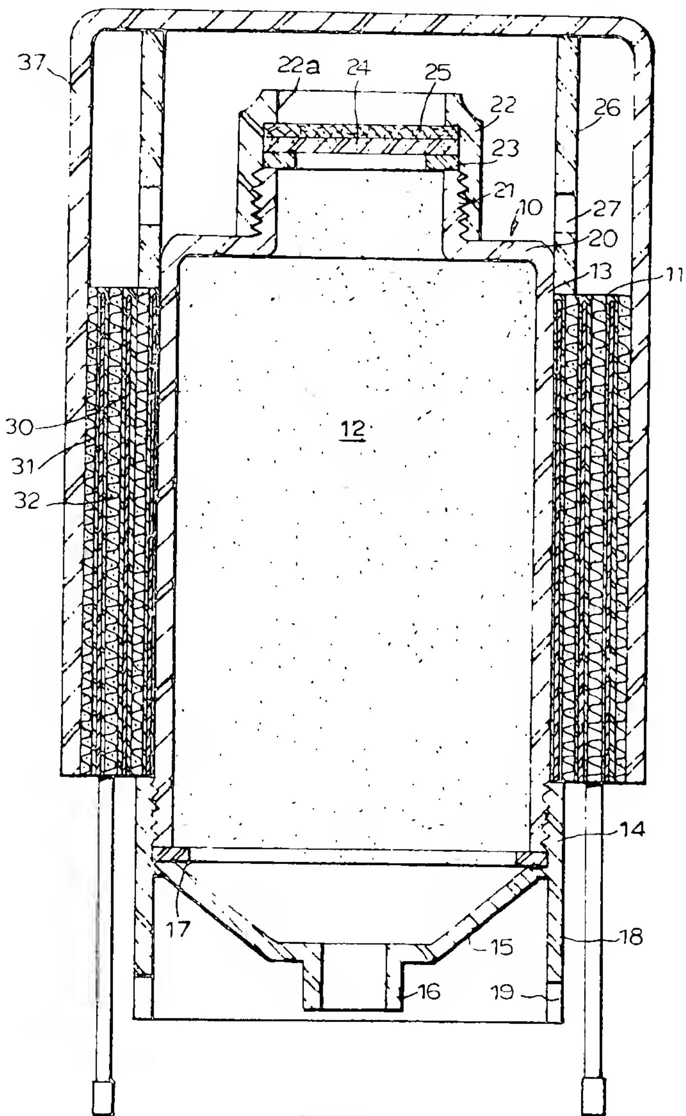

FIG.2

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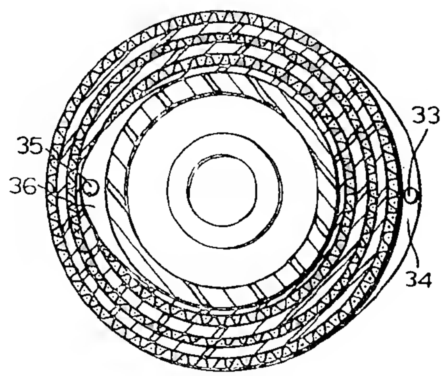

FIG.3

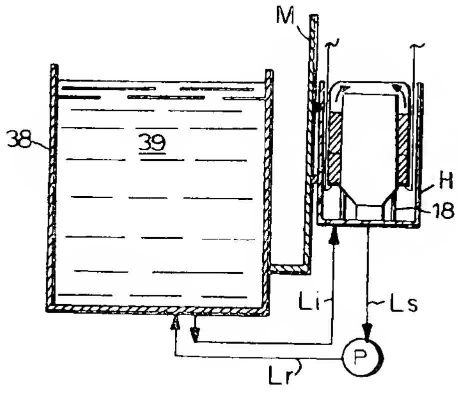

FIG.4

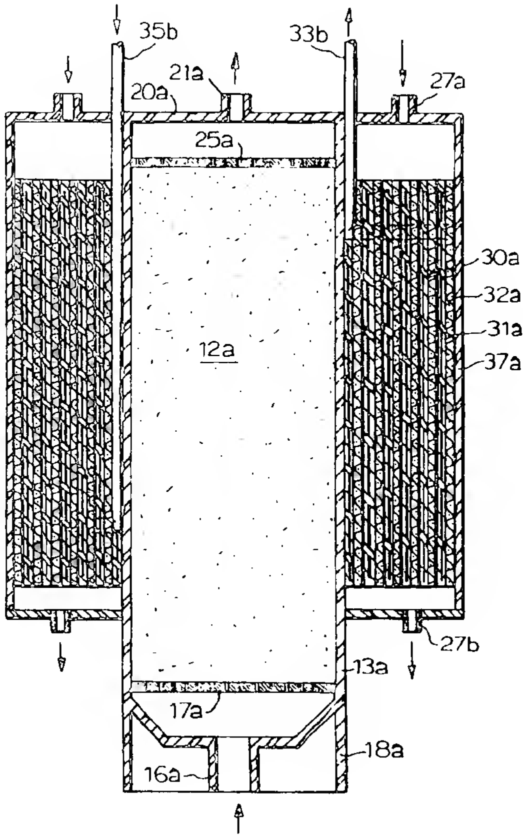

FIG. 5

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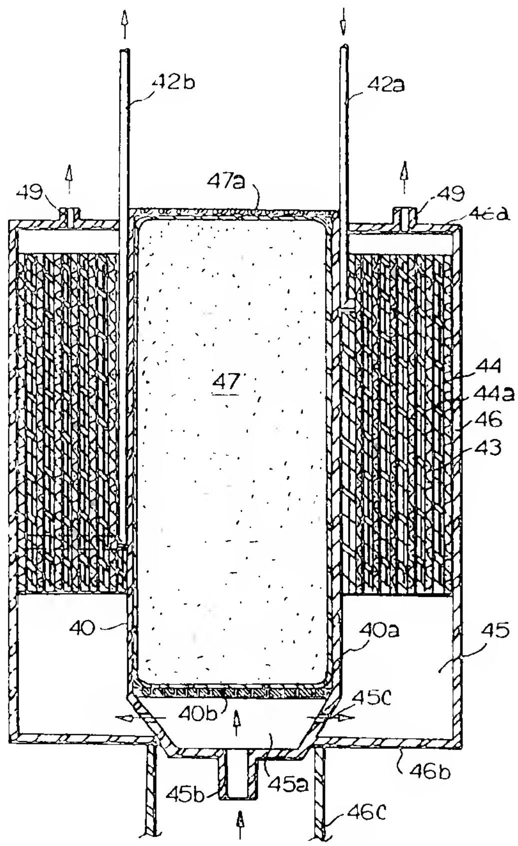

FIG. 6

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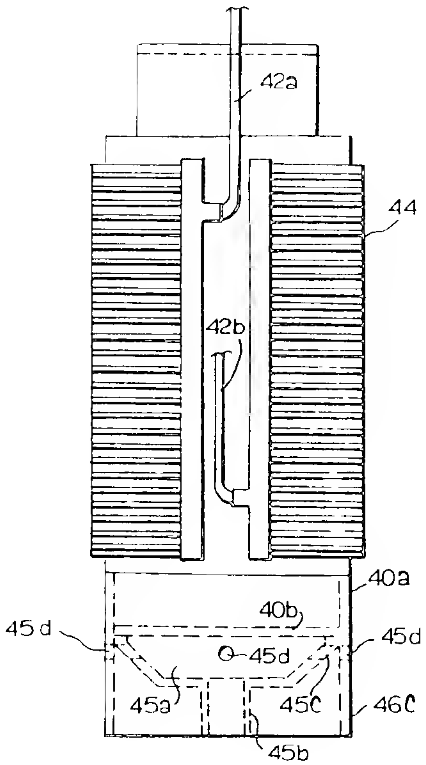


FIG. 8

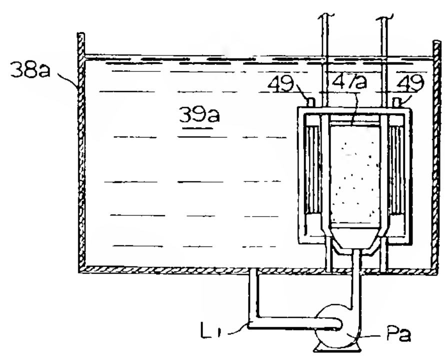
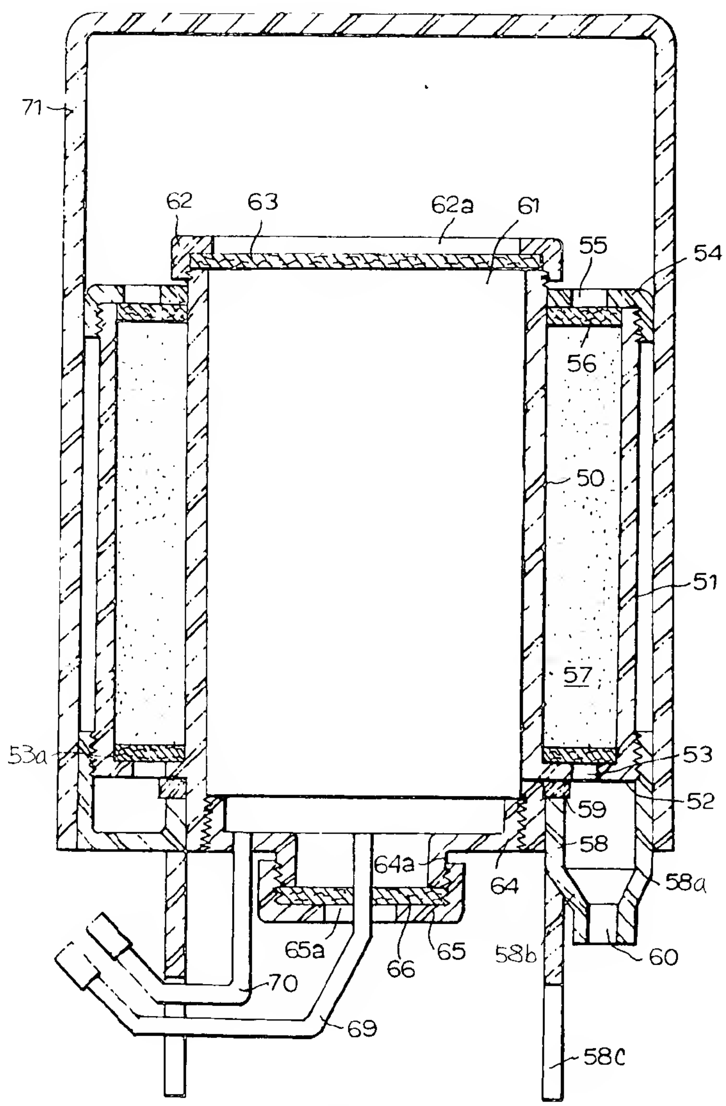


FIG. 7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58b
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58c

FIG. 9

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Sheet 8

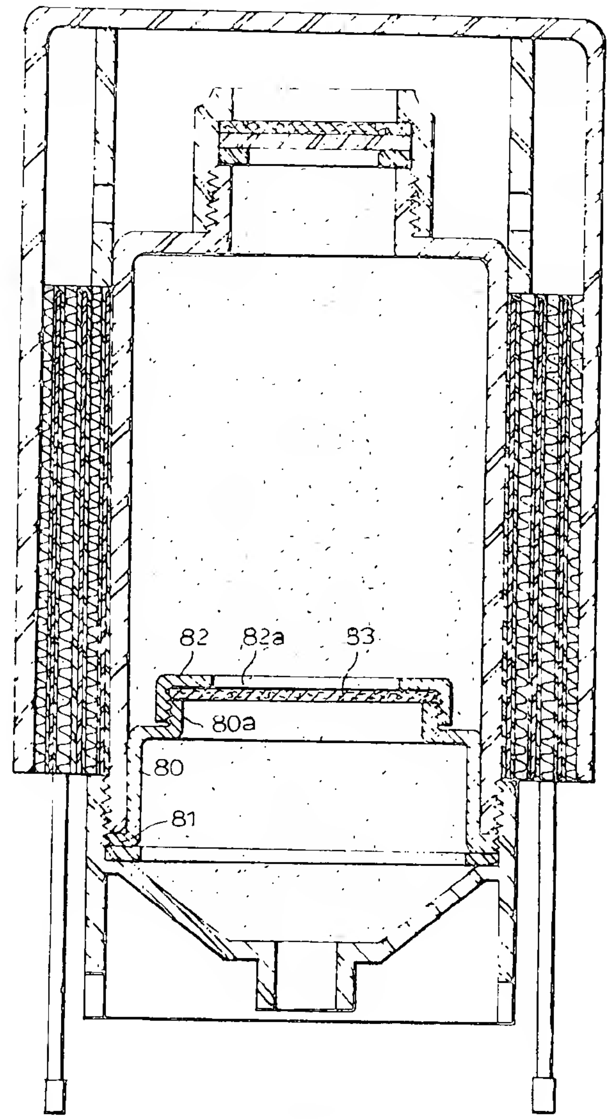


FIG.10

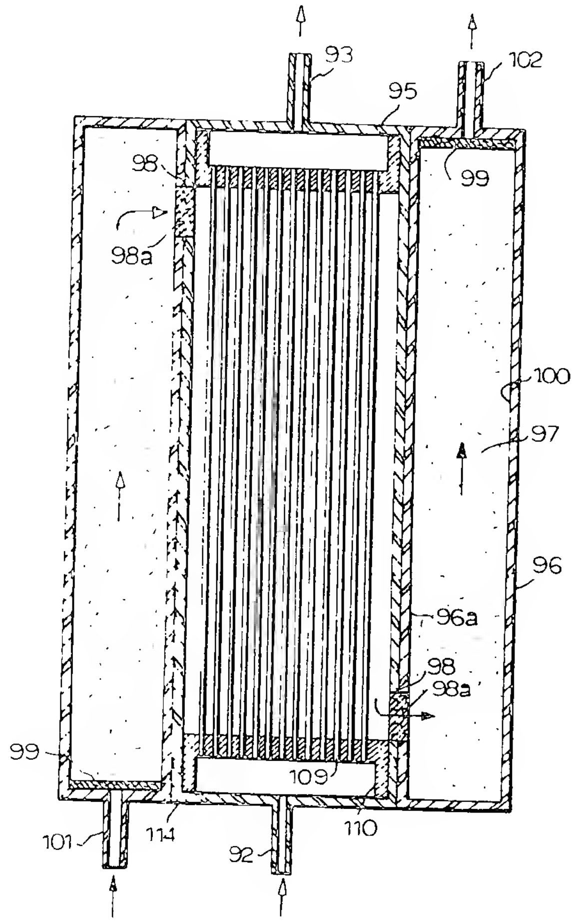
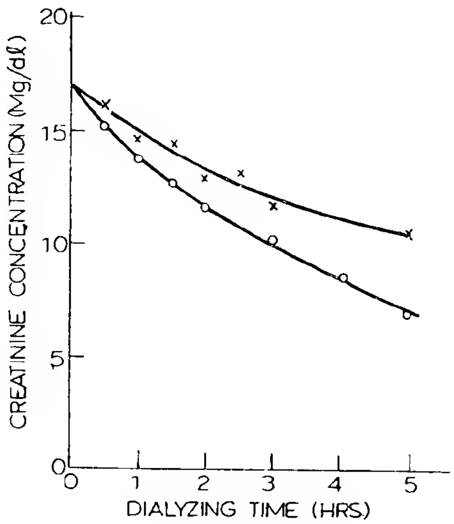


FIG.11


CREATININE CONCENTRATION (Mg/dℓ)
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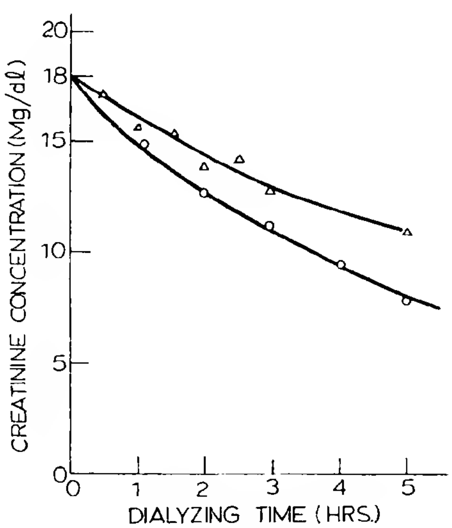
15
10
5
0
0
1
2
3
4
5
DIALYZING TIME (HRS)

FIG. 13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20
18
15
10
5
0
0
1
2
3
4
5
DIALYZING TIME (HRS.)

FIG. 12